Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
PH-2079-PCT		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/004698	31.03.2004	31.03.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant		
KIRIN BEER KABUSHIKI KAISHA		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 10 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☒ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/004698

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 12-24

because:

☒ the said international application, or the said claims Nos. 12-24 relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matter of claims 12-24 pertains to a method for treatment of the human body by therapy.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 12-24

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted the claims nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☒ not complied with for the following reasons:

   (Continued on supplemental sheet)

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. _____

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	26	YES
	Claims	1-11, 25	NO
Inventive step (IS)	Claims		YES
	Claims	1-11, 25, 26	NO
Industrial applicability (IA)	Claims	1-11, 25, 26	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: JP 2-503514 A (Waldmann, Herman), 25 October 1990, entire document; page 3, lower right column, lines 9 to 14 & EP 328404 A1 & WO 89/7452 A1 & GB 2216126 A & AU 8930626 B & US 5846534 A & JP 11-228900 A

Document 2: MASUYAMA J. et al., 'A novel costimulation pathway via the 4C8 antigen for the induction of CD4+ regulatory T cells', J. Immunol., (2002), Vol. 169, No.7, pages 3710 to 3716

Document 3: WO 02/30460 A2 (ISIS INNOVATION LTD.), 18 April 2002, entire document & AU 2001/93995 B & EP 1324771 A1 & JP 2004-510827 A

Document 4: WO 00/10603 A1 (UNIV LELAND STANFORD JUNIOR),02 March, 2000, entire document & EP 1107789 A1 & JP 2004-503463 A

Document 5: JP 2000-506723 A (ISIS INNOVATION LTD.), 6 June 2000, entire document & WO 97/31024 A1 & AU 9718851 B & EP 970127 A1 & US 2002/48578 A

[1]

Document 1 sets forth an Campath-1 antibody (which

is understood to correspond to "a CD52 agonist other than 4C8 antibody") has been employed as an active ingredient of an immunosuppressive drug in the past. Document 1 also sets forth a human antibody to said antibody and a method of producing said human antibody.

Therefore the inventions set forth in claims 1 to 11 and 25 are disclosed in document 1, and hence lack novelty and do not involve an inventive step.

[2]

Documents 1 to 5 set indicate that an antibody of Campath-1 antibody which is an antibody to the CD52 antibody (Documents 1 and 3 to 5) and a 4C8 antibody (document 2) (which both correspond to a "CD52 agonist")offers an immunosuppressive effect and an effect of inducing the differentiation' and/or promoting the proliferation of regulatory T cells. In the light of these documents, it would be easy for a person skilled in the art to select by screening a CD52 antibody other than the aforementioned antibodies which has a similar activity as a marker for interaction with CD52.

Therefore the invention set forth in claim 26 does not involve an inventive step in the light of document 1.

[3]

Documents 3 to 5 set forth a humanized antibody of Campath-1 antibody and a method of producing said human antibody.

Therefore the invention set forth in claims 25 is disclosed in documents 3 to 5, and hence lacks novelty and does not involve an inventive step.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
JP 2003-102471 A (E,X)	08.04.2003	01.10.2001	

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1 to 9 and 11 relate to medicinal compositions for immunosuppression which contain, as the active ingredient, a compound having a desired property as "a CD52 agonist" other than 4C8 antibody. Although claims 1 to 9 and 11 involve any compounds having the property as "a CD52 agonist" as described above, only the employment of a publicly known Campath-1 antibody, among the claimed compounds, is supported by the description within meaning of PCT Article 6 and disclosed therein within the meaning of PCT Article 5.

Even though the common technical knowledge at the point of the application is taken into consideration, the space of the compounds having the property as "a CD52 agonist" cannot be specified. Thus, the above claims do not comply with the requirement of clearness within PCT Article 6 too.

Such being the case, the opinion was formed based on the results of a prior art which was carried out mainly on the Campath-1 antibody as set forth in claim 10 which is employed in practice in the description as "a CD52 agonist" other than 4C8 antibody, and an immunosuppressive drug having said antibody as an active ingredient.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of:

(Continued from Box IV.3)

[1] Claims 1 to 11: (referred to as the invention group [I])

[2] Claim 25 : (referred to as the invention group [2])

[3] Claim 26 : (referred to as the invention group [3])

The matter specifying invention common to the invention groups [1] to [3] exclusively resides in a drug having an immunosuppressive effect.

However, the following drug:

• an immunosuppressive drug containing as the active ingredient a humanized antibody of Campath-1 antibody (seemingly corresponding to "a CD52 agonist other than 4C8 antibody" as specified in the invention group [1], and to "an anti-CD52 humanized antibody usable as a drug having an immunosuppressive effect and an effect of inducing the differentiation and/or promoting the proliferation of regulatory T cells… " as specified in the invention group [2]):

is reported in the documents cited in the column C, for example;

(*) JP 2-503514 A (Waldman and Harman) 1990.10.25, entire document, page 3, right lower column, lines 9-14 & EP 328404 Al & WO 89/7452 Al & GB 2216126 A & AU 8930626 B & US 5846534 A & JP 11-228900 A

Moreover, a humanized antibody of Campath-1 and a process for producing the same are illustrated in the documents cited in column C:

(*) WO 02/30460 A2 (ISIS INNOVATION LTD) 2002.04.18, the entire document & Au 2001/93995 B & EP 1324771 Al & JP

Supplemental Box

2002-510827 A

(*) WO 00/10603 A1 (UNIV LELAND STANFORD JUNIOR) 200.03.02, the entire document & EP 1107789 A1 & JP 2004-503463A

(*) JP2000-506723A (ISIS INOVATION LTD) 2000.06.06, the entire document & WO 97/31024 A1 & AU 9718851 B & EP 970127 A1 & US 2002/48578 A

and, therefore, were publicly known before the priority date of the present case.

A 4C8 antibody (seemingly corresponding to "a drug having an immunosuppressive effect and an effect of inducing the differentiation and/or promoting the proliferation of regulatory T cells..." as specified in the invention group [3]) is also reported in the documents cited in the column C, for example;

(*) MASUYAMA, J. et al., "A novel costimulation pathway via the 4Claim 8 antigen for the induction of CD4+ regulatory T cells" J. Immunol., (2002) vol. 169, no.7, p.3710-3716

Based on the statements in these documents, it appears that there is no special technical feature common to the invention groups [1] to [3] and thus these groups of inventions cannot be considered as a group of inventions so linked as to form a single general inventive concept.